

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US2004/029293

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 G01N33/74 A61K31/194 A61K31/4196 A61K31/445 A61K31/4453
A61K31/45 A61P9/08 A61P9/10 A61P3/10 A61P35/00
A61P9/02

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 G01N A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, BEILSTEIN Data, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category * | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
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| X | <p>LOOKER, J. H. ET AL: "1,2,3-Thiadiazoles as potential antineoplastic agents. I. Synthesis of novel 4-monosubstituted and 4,5-disubstituted derivatives Physiologically active compounds. III. Hydrochlorides of amino esters of phenylcyclohexylglycolic acids, of amides of benzilic, phenylcyclohexyl- and dicyclohexylglycolic," JOURNAL OF HETEROCYCLIC CHEMISTRY, 2(4), 348-54 CODEN: JHTCAD; ISSN: 0022-152X, 1965, XP002314287 page 352, left-hand column, line 6 - line 12; table I</p> <p style="text-align: center;">----- -/--</p> | 9, 10, 17-19, 53, 54 |

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents :

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- *&* document member of the same patent family

Date of the actual completion of the international search

13 June 2005

Date of mailing of the international search report

01. 07. 2005

Name and mailing address of the ISA

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Authorized officer

Fausti, S

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| C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT | | |
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| Category * | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
| X | <p>TMEJ C ET AL: "A COMBINED HANSCH/FREE-WILSON APPROACH AS PREDICTIVE TOOL IN QSAR STUDIES ON PROPAFENONE-TYPE MODULATORS OF MULTIDRUG RESISTANCE" ARCHIV DER PHARMAZIE, VCH VERLAGSGESELLSCHAFT MBH, WEINHEIM, DE, vol. 331, no. 7/8, 1998, pages 233-240, XP000881287 ISSN: 0365-6233 abstract; page 233, left-hand column, first paragraph; tables 1-2; figure 1</p> <p style="text-align: center;">-----</p> | 9,10, 17-19, 53,54 |
| X | <p>MURAD S ET AL: "STRUCTURE-ACTIVITY RELATIONSHIP OF MINOXIDIL ANALOGS AS INHIBITORS OF LYSYL HYDROXYLASE IN CULTURED FIBROBLASTS1" ARCHIVES OF BIOCHEMISTRY AND BIOPHYSICS, NEW YORK, US, US, vol. 292, no. 1, 1992, pages 234-238, XP000564071 ISSN: 0003-9861 abstract; table I; page 237, paragraph joining left- and right-hand columns; paragraph joining pages 237 and 238</p> <p style="text-align: center;">-----</p> | 9,10,53, 54 |
| X | <p>EAKIN A E ET AL: "COMPARATIVE COMPLEMENT SELECTION IN BACTERIA ENABLES SCREENING FOR LEAD COMPOUNDS TARGETED TO A PURINE SALVAGE ENZYME OF PARASITES" ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, AMERICAN SOCIETY FOR MICROBIOLOGY, WASHINGTON, DC, US, vol. 39, no. 3, March 1995 (1995-03), pages 620-625, XP001055590 ISSN: 0066-4804 abstract; table 2</p> <p style="text-align: center;">-----</p> | 9,10,53, 54 |
| X | <p>FR 2 241 313 A (SANDOZ S.A.) 21 March 1975 (1975-03-21) claims 1,13,14</p> <p style="text-align: center;">-----</p> | 9,10,53, 54 |
| P,X | <p>MARTÍNEZ A ET AL: "Identification of vasoactive nonpeptidic positive and negative modulators of adrenomedullin using a neutralizing antibody-based screening strategy" ENDOCRINOLOGY 2004 UNITED STATES, vol. 145, no. 8, August 2004 (2004-08), pages 3858-3865, XP009042699 ISSN: 0013-7227 abstract; figure 6; tables 1,2</p> <p style="text-align: center;">-----</p> <p style="text-align: center;">-/--</p> | 1-75 |

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

| Category * | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
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| P, X | <p>GASPARETTO M ET AL: "Identification of compounds that enhance the anti-lymphoma activity of rituximab using flow cytometric high-content screening" JOURNAL OF IMMUNOLOGICAL METHODS, ELSEVIER SCIENCE PUBLISHERS B.V.,AMSTERDAM, NL, vol. 292, no. 1-2, September 2004 (2004-09), pages 59-71, XP004550500 ISSN: 0022-1759 abstract; table 1</p> | <p>9,10, 20-28, 53,54</p> |
| A | <p>WO 97/07214 A (UNSWORTH EDWARD J ; MACRI CHARLES (US); US HEALTH (US); CUTTITTA FRANK) 27 February 1997 (1997-02-27)</p> <p>abstract</p> | <p>1-4, 9-28,47, 48, 51-54, 57,58,61</p> |
| A | <p>EGUCHI SATORU ET AL: "Structure-activity relationship of adrenomedullin, a novel vasodilatory peptide, in cultured rat vascular smooth muscle cells" ENDOCRINOLOGY, BALTIMORE, MD, US, vol. 135, no. 6, 1994, pages 2454-2458, XP002193142 ISSN: 0013-7227 abstract</p> | <p>1-4, 9-28,47, 48, 51-54, 57,58,61</p> |
| A | <p>AMIR S M ET AL: "POLYPHLORETIN PHOSPHATE AN ANTAGONIST OF THYROTROPIN ACTION EVIDENCE FOR AN INTERACTION WITH THE HORMONE RATHER THAN THE RECEPTOR" ENDOCRINOLOGY, vol. 117, no. 3, 1985, pages 860-868, XP009042800 ISSN: 0013-7227 abstract</p> | |
| A | <p>HEUSER MARKUS ET AL: "The inhibition of angiogenesis and microcirculation in renal cell carcinoma spheroids by gastrin releasing peptide receptor (GRP-R) antagonism depends on the time of treatment initiation." JOURNAL OF UROLOGY, vol. 169, no. 4 Supplement, April 2003 (2003-04), page 207, XP009042804 & 98TH ANNUAL MEETING OF THE AMERICAN UROLOGICAL ASSOCIATION (AUA); CHICAGO, IL, USA; APRIL 26-MAY 02, 2003 ISSN: 0022-5347 abstract</p> | |

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

| Category * | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
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| X | <p>DATABASE CA 'Online! CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; 1964, CHERNOV, V. A. ET AL: "Antiblastomic activity of sydnone imines" XP002331366 retrieved from STN Database accession no. 1964:406942 abstract & DOKLADY AKADEMII NAUK SSSR , 155(1), 216-19 CODEN: DANKAS; ISSN: 0002-3264, 1964,</p> | <p>9,10, 35-37, 55,56,61</p> |
| X | <p>DAENIKER, H. U. ET AL: "Chemotherapeutic studies in the heterocyclic series. XVIII. Polymethylenedi(sydnone)s and polymethylenedi(hydrazines)" HELVETICA CHIMICA ACTA , 40, 918-32 CODEN: HCACAV; ISSN: 0018-019X, 1957, XP009048688 compound IVa on page 920; last paragraph (foot notes) on page 925</p> | <p>9,10, 35-37, 55,56,61</p> |
| X | <p>THOMAS F ET AL: "ANTITUMORAL ACTIVITY OF BOMBESIN ANALOGUE ON SMALL CELL LUNG CANCER XENOGRAFTS RELATIONSHIP WITH BOMBESIN RECEPTOR EXPRESSION" CANCER RESEARCH, vol. 52, no. 18, 1992, pages 4872-4877, XP001206441 ISSN: 0008-5472 abstract</p> | <p>65</p> |
| P,X | <p>BAJO A M ET AL: "BOMBESIN ANTAGONISTS INHIBIT PROANGIOGENIC FACTORS IN HUMAN EXPERIMENTAL BREAST CANCERS" BRITISH JOURNAL OF CANCER, LONDON, GB, vol. 90, no. 1, 12 January 2004 (2004-01-12), pages 245-252, XP001183666 ISSN: 0007-0920 abstract</p> | <p>62-65</p> |
| A | <p>CUTTITTA F ET AL: "BOMBESIN-LIKE PEPTIDES CAN FUNCTION AS AUTOCRINE GROWTH FACTORS IN HUMAN SMALL-CELL LUNG CANCER" NATURE (LONDON), vol. 316, no. 6031, 1985, pages 823-826, XP001206814 ISSN: 0028-0836 page 823, right-hand column, second paragraph; page 824, left-hand column, second paragraph; figure 3; page 826, left-hand column, lines 1-4</p> | <p>5-8, 29-46, 49-52, 55,56, 59-61</p> |

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

| Category * | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
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| A | ASHWOOD V ET AL: "PD 176252 - The First High Affinity Non-peptide Gastrin-Releasing Peptide (BB2) Receptor Antagonist" BIOORGANIC & MEDICINAL CHEMISTRY LETTERS, OXFORD, GB, vol. 8, no. 18, 22 September 1998 (1998-09-22), pages 2589-2594, XP004138276 ISSN: 0960-894X abstract | 5-8, 29-46, 49-52, 55,56, 59-61 |
| X | ----- WO 99/05299 A (TRUSTEES OF BOSTON UNIVERSITY) 4 February 1999 (1999-02-04) claims 16,27,40 | 9,10, 35-37, 55,56,61 |
| X | ----- WO 00/30630 A (LINDEN BIOTECHNOLOGY, INC; XIA, ZHI-TAO) 2 June 2000 (2000-06-02) claim 9; figure 1 | 9,10, 35-37, 55,56,61 |
| A | ----- EP 0 806 418 A (NIPPON SHOJI KAISHA, LIMITED) 12 November 1997 (1997-11-12) abstract; claims 5-10; table 22; compound 105 | 49,59, 66-75 |
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Box II Observations where certain claims were found unsearchable (Continuation of Item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Although claims 11-46 and 62-75 are directed to a method of treatment of the human/animal body, the search has been (could be) carried out and based on the alleged effects of the compounds.
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box III Observations where unity of invention is lacking (Continuation of Item 3 of first sheet)

This International Searching Authority found multiple inventions in this International application, as follows:

see additional sheet

1. ☒ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☒ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims:

1-4, 9-28, 47-48, 51-52(partially), 53-54,
57-58, 61(partially)

Non-peptidic adrenomedullin modulators, which bind to the hormone moiety, complexes thereof and their medical and analytical uses/kits.

2. claims:

5-8, 29-46, 49-50, 51-52(partially), 55-56,
59-60, 61-64(partially), 66-75

Non-peptidic gastrin-releasing peptide (GRP) modulators, which bind to the hormone moiety, complexes thereof and their medical and analytical uses/kits.

3. claims: 62-64 (evtl. also 66-72)

Medical use of GRP inhibitors for non tumour-related angiogenesis.

4. claim: 65 (evtl. also 73)

Medical use of GRP inhibitors for tumour-related angiogenesis.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/US2004/029293

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